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NON-HODGKIN'S LYMPHOMAS IN US NAVY PERSONNEL(U) NAVAL
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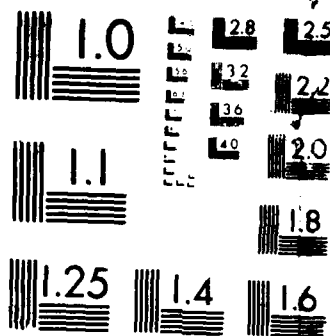
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NON-HODGKIN'S LYMPHOMAS IN U.S. NAVY PERSONNEL

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REPORT NO. 86-26

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NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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Non-Hodgkin's Lymphomas in U.S. Navy Personnel*

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Summary

Non-Hodgkin's lymphomas are one of the most commonly occurring cancers in the age-groups heavily represented in the U.S. Navy. The Navy has a wide range of potential occupational exposures. This study was initiated to identify any occupational associations of non-Hodgkin's lymphomas that may adversely affect naval readiness.

The objective of this study was to compare the incidence of non-Hodgkin's lymphomas in U.S. Navy active-duty enlisted personnel during the period 1974-83 with the general U.S. population; and to assess if risk varied by naval occupation or length of service.

The Naval Health Research Center's computer-based disease registry was used to conduct a prospective study of all white U.S. Navy enlisted men during 1974-83 to test for the existence of any short-term risk possibly due to occupation. Men in 80 occupations, ranging from clerk to journalist to machinist and boiler operator were observed for 3,704,864 person-years; mean length of service was 5.1 years, but 19 percent of person-years were contributed by men who had served at least 11 years. Incident cases of non-Hodgkin's lymphomas were identified and verified using Medical Board findings or review of original medical records. Average-annual age-specific and age-adjusted incidence rates were calculated. Expected numbers of cases for each occupational group were derived using U.S. rates provided by Surveillance, Epidemiology, and End Results (SEER), Incidence and Mortality Data, 1973-81. Standardized incidence ratios were calculated for all Naval occupations with at least one case of non-Hodgkin's lymphoma, and statistical significance was assessed using the Poisson distribution.

Examination of pathology records and medical review boards confirmed 68 cases of non-Hodgkin's lymphomas. The annual age-adjusted incidence rate per 100,000 person-years in Navy men was significantly lower than in the U.S. SEER population, probably due to screening and other selection factors associated with Navy service that result in a healthy worker effect. Risk was unrelated to length of service, and no occupational groups showed a significant excess risk.

Results of this study indicate there is no overall or occupation-specific increase in risk of non-Hodgkins lymphomas in the U.S. Navy which was detectable in this relatively short-term prospective study.

Non-Hodgkin's Lymphomas in U.S. Navy Personnel

Frank C. Garland, Edward D. Gorham, Cedric F. Garland, and Jay Ferns

Introduction

There were 27,200 new cases of non-Hodgkin's lymphomas and 14,600 deaths in the United States in 1986 (1). The incidence of this heterogeneous group of disorders has virtually doubled during the past two decades where careful studies of incidence have been performed, such as the Yorkshire health region of England (2,3). Although the causes of this group of malignancies are largely unknown, several studies indicate associations with occupational (3-14) or environmental (15) exposures. We report here the results of a prospective study of the effect of occupation on short-term risk of these malignancies in white U.S. Navy enlisted men during 3,704,864 person-years in 80 occupations between January 1, 1974 and December 31, 1983. The occupations ranged from clerical work (e.g., personnelmen and data systems technicians), to medical care (e.g., hospital corpsmen), to industrial work (e.g., boiler technicians, machinist's mates, and hull maintenance technicians), with corresponding exposures.

Excess death rates from reticulum-cell sarcoma (Standardized Mortality Ratio [SMR] = 1.7, $p < 0.01$) and lymphosarcoma (SMR = 2.1, $p < 0.01$) were reported in males aged 0-45 years who worked in occupations using benzene in New York State exclusive of New York City (4). A 1.5-fold excess of fatal non-Hodgkin's lymphoma was reported in white male workers at a rubber factory (5,6) and a small excess was observed in uranium mill workers (7). Both population-based case-control studies (8,9) and a prospective study (10) have suggested an association between occupational exposure to phenoxyacetic acid herbicides and non-Hodgkin's lymphomas (11).

Although proportionate mortality studies must be interpreted with caution, several have reported an excess in per cent of deaths from non-Hodgkin's lymphomas in chemists. Proportionate mortality for fatal lymphoid malignancies in chemists who were members of the American Chemical Society (the principal professional society in the field) was 1.8 times greater than expected for their age and demographic characteristics ($p < 0.001$)(12). A high proportionate mortality from lymphoma was also reported in members of

the British Royal Institute of Chemistry (13) and in Swedish chemists (14). Environmental exposure to organic solvents in the vicinity of a chemical plant also has been suggested as being associated with risk of non-Hodgkin's lymphoma (15). Finally, the possibility of a retroviral or other infectious etiology in the non-Hodgkin's lymphomas is a question of increasing importance which might be relevant to those in health care professions (16,17).

Since naval personnel perform many occupations requiring use of industrial chemicals and others serve as hospital corpsmen, they were studied for risk of non-Hodgkin's lymphomas in comparison with the U.S. population in the Surveillance, Epidemiology, and End Results program of the U.S. National Cancer Institute (18).

Subjects and Methods

All white male enlisted men who served in the Navy during January 1, 1974, through December 31, 1983, were ascertained from a continuously updated file providing age, race, sex, educational level, length of service, and occupation. Mean annual population size was 435,425 active-duty men; the denominator for the study was the 3,704,864 person-years experienced by these men.

All cases of non-Hodgkin's lymphomas were ascertained through search of a registry which listed detailed information on all hospitalizations, medical review board findings, and deaths during the period of active duty. The study was confined to events which occurred in active-duty personnel, since data were not available on incidence after discharge from the Navy. All first hospitalizations of white men diagnosed as having non-Hodgkin's lymphomas (ICDA-8 codes 200.0, 200.1, 202.0-202.9 and ICDA-9 codes 200.0, 200.1, 202.1, 202.8, 202.9) were identified for the period 1974-83. In order to confirm the diagnoses, original medical records were obtained from the National Personnel Records Center in St. Louis, Missouri, U.S.A. or from the hospital where the diagnosis was made. When a diagnosis of lymphatic malignancy is made in the Navy, microscopic examination of the pathologic tissue is performed and the diagnosis is verified by a medical review board consisting of at least two physicians, including a specialist in the disease.

Of the original 103 first hospitalizations identified 35 cases were excluded: 3 who had received a diagnosis prior to January 1, 1974; 17 who had a final diagnosis other than a non-Hodgkin's lymphoma; and 15 who lacked pathological verification of a diagnosis and whose diagnosis could not be verified from pathology records in any tumor registry of a major continental U.S. Naval hospital (Bethesda, Maryland; San Diego, California; Oakland, California; or Portsmouth, Virginia). This report is based on the 68 remaining cases, all confirmed either through pathology reports present in the medical or tumor registry record (N = 51) or reports from medical review boards (N = 17).

Denominators were obtained from a career history file which provided the annual population of all active-duty men by age, race, sex, length of service, and occupation. Age-adjustment of the incidence rate for each occupation was done using the indirect method since the number of cases in some age categories was not large enough to provide the stability appropriate for direct adjustment. Standardized incidence ratios (SIRs) were calculated for each occupation having at least one case of non-Hodgkin's lymphoma, using expected values based on annual age-, race-, and sex-specific rates for the entire Navy, and U.S. rates provided by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program (18). The SEER incidence rate is a weighted average of two time periods, 1973-77 and 1978-81. The Poisson distribution was used to calculate exact p-values and 95 percent confidence limits on SIRs (19, 20). All p-values reported are two-sided.

Results

The distribution of cases is shown in Table 1 according to diagnosis (21). Diffuse histiocytic non-Hodgkin's lymphoma was the most frequently detected category (36.8%).

Age-specific incidence rates of non-Hodgkin's lymphoma were lower in Navy men, and the annual age-adjusted incidence rate was significantly lower ($p < 0.05$) than the rate in the U.S. SEER population (Table 2). There was no evidence of an increase in age-adjusted incidence rates with length of service (Table 3).

Table 1
Diagnostic classification of non-Hodgkin's lymphomas
in active-duty enlisted U.S. Naval personnel,
white males, 1974-83

<u>ICD-9* classification (codes)</u>	<u>Description†</u>	<u>No.</u>	<u>%</u>
Reticulosarcoma/lymphosarcoma (200.0-1)	<u>Diffuse lymphoma</u>		
	Histiocytic	25	36.8
	Lymphocytic poorly differentiated	6	8.8
	Undifferentiated, pleiomorphic	5	7.4
	Lymphocytic well differentiated	4	5.9
	Mixed lymphocytic histiocytic	4	5.9
Nodular lymphoma (202.0)	<u>Nodular lymphoma</u>		
	Lymphocytic poorly differentiated	10	14.7
	Mixed lymphocytic histiocytic	3	4.4
Mycosis fungoides (202.1)	<u>Mycosis fungoides</u>	1	1.5
Leukemic reticuloendo- theliosis (202.4)	<u>Hairy cell leukemia</u>	3	4.4
Other lymphoma, NOS‡(202.8-9)	<u>Other lymphoma, NOS‡</u>	7	10.2
Total		68	100.0

*International Classification of Diseases, 9th Revision.

†Rappaport nomenclature (21).

‡NOS, not otherwise specified

Standardized incidence ratios were obtained for all U.S. Naval occupations with at least one case of non-Hodgkin's lymphoma. Significant SIRs were not observed in any occupation, but occupational groups with a suggestive SIR of 1.5 or higher are shown in Table 4. All occupations which experienced 1 or more cases during 1974-83 are shown in the Appendix. Examination of the data for a secular trend during 1974-83 revealed no

Table 2

Age-specific and age-adjusted incidence rates and 95 percent confidence limits for non-Hodgkin's lymphomas per 100,000 person-years, active-duty U.S. Naval personnel and United States SEER population, white males, 1974-83

Age (years)	U. S. Naval personnel				U.S. SEER incidence rate*
	Person- years at risk	No. of cases	Average annual rate	(95 percent confidence limits)	
17 - 19	664,255	6	0.9	(0.3 - 1.9)	1.5
20 - 29	2,208,270	27	1.2	(0.8 - 1.8)	2.1
30 - 39	709,138	28	3.9	(2.6 - 5.7)	4.0
40 - 49	105,969	7	6.6	(2.7 - 13.6)	9.6
50 - 64	7,604	0	-	-	23.9
Unknown	9,628	0	-	-	-
Total	3,704,864	68	1.8	(1.4 - 2.4)	9.9
Age-adjusted rate			6.9†	(5.4 - 8.9)	9.9

*Weighted average for periods 1973-77 and 1978-81.

†Adjusted by the indirect method using SEER incidence rates applied to the Navy population. Statistically significant at the $p < 0.05$ level.

evidence of an increase or decrease in incidence during this period (not shown).

Table 3

Age-adjusted incidence rates and 95 percent confidence limits
 for non-Hodgkin's lymphomas per 100,000 person-years,
 by years of service, active-duty
 U.S. Naval personnel, white males, 1974-83

<u>Years of service</u>	<u>Person- years at risk</u>	<u>No. of cases</u>	<u>Crude incidence rate</u>	<u>Age-adjusted incidence</u>	
				<u>Average annual rate</u>	<u>95 percent confidence limits</u>
0.0 - 1.9	1,194,584	9	0.8	4.6	(2.1 - 8.7)
2.0 - 3.9	915,049	14	1.5	8.5	(4.6 - 14.3)
4.0 - 6.9	531,231	8	1.5	6.9	(2.9 - 13.6)
7.0 - 10.9	364,947	4	1.1	3.9	(1.1 - 9.9)
11.0+	699,060	33	4.7	9.6	(6.5 - 13.5)
Unknown	9,628	0	-	-	-
<hr/>					
Total	3,704,864	68	1.8	6.9*	(5.4 - 8.9)

*Adjusted by the indirect method using SEER incidence rates applied to the naval population. Statistically significant at the $p < 0.05$ level.

Table 4
Standardized Incidence Ratios (SIRs) for non-Hodgkin's
lymphomas by U.S. Navy occupation, white male, enlisted
active-duty personnel, 1974-83

<u>Occupation*</u>	<u>No. of cases</u>	<u>SIR†</u>	<u>95% confidence limits</u>
Mess management specialist	4	1.9	(0.5 - 4.9)
Airman	5	1.9	(0.5 - 4.4)
Aviation ASW‡ operator	2	1.6	(0.3 - 9.4)
Boatwain's mate	4	1.7	(0.5 - 4.4)
Interior communications electrician	2	1.7	(0.2 - 6.1)
Aviation structural mechanic	5	1.5	(0.5 - 3.5)

*Includes only occupations with SIRs of 1.5 or larger and with 2 or more cases.

†Expected numbers of cases are based on incidence rates provided by Surveillance, Epidemiology and End Results (SEER) Program, 1973-81.

‡ASW, anti-submarine warfare.

Discussion

The advantages and disadvantages of the medical records system used in this study are similar to those of a community-based cancer registry which collects data from a well-defined but mobile population (22). Assuring accuracy of the diagnosis is a particular problem in entities such as non-Hodgkin's lymphomas. The problem exists in any registry-based surveillance

system, but examination of corroborating evidence, including original medical records, medical review board findings and microscopic tissue examination greatly minimized this source of error.

Studies of working populations such as active-duty military personnel are most appropriate for diseases with relatively short latency periods. This study was confined to personnel on active duty, and no data were available which could be used to determine incidence rates in persons who had become separated from the Navy. While a healthy worker effect may have existed in this study, it was not present in previous studies of Hodgkin's disease (25) and testicular cancer (26) using the same methods of case ascertainment and verification over a similar time period.

Negative studies are of value as guides to future research. This detailed examination of a wide variety of occupations showed no occupational associations to suggest possible risk factors for non-Hodgkin's lymphomas in the short-term. Follow-up studies of populations such as this for incidence and mortality in the long-term (greater than 20 years) are needed.

The age-adjusted male:female ratio for incidence of non-Hodgkin's lymphomas in the U.S.A. is about 1.1 (23). Male:female ratios for mortality in U.S. whites at ages 0-19, and 20-54, and 55+ are 2.3 and 1.6, and 1.4, respectively (24). The absence of a male excess in the incidence data and the decline in the male:female mortality ratio with increasing age suggests that the non-Hodgkin's lymphomas as a group may not be due mainly to exposures to occupations which have traditionally over-represented men, such as heavy industry, but rather to exposures equally common to both sexes, such as infections, diet, behavior, or general environmental exposures. Recent increases in incidence (2,3) suggest either that diagnosis has vastly improved or that a new exposure is occurring.

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APPENDIX

Standardized incidence ratios (SIR) for non-Hodgkin's lymphomas for occupations with at least one case, active-duty enlisted U.S. Naval personnel, white males, 1974-83

<u>Occupation</u>	<u>No. of cases</u>	<u>SIR</u>	<u>95% confidence limits</u>
Journalist	1	5.3	(0.1 - 29.5)
Missile technician	1	2.6	(0.1 - 14.5)
Navy counselor	1	2.3	(0.1 - 12.8)
Electronics warfare technician	1	2.3	(0.1 - 12.8)
Aviation support equipment technician	1	2.0	(0.0 - 11.1)
Photographer's mate	1	2.0	(0.0 - 11.1)
Airman	5	1.9	(0.6 - 4.4)
Mess management specialist	4	1.9	(0.5 - 4.9)
Machinery repairman	1	1.8	(0.0 - 10.0)
Boatswain's mate	4	1.7	(0.5 - 4.4)
Interior communications electrician	2	1.7	(0.2 - 6.1)
Aviation ASW* operator	2	1.6	(0.3 - 9.4)
Aviation structural mechanic	5	1.5	(0.5 - 3.5)
Signalman	1	1.5	(0.0 - 8.4)
Personnelman	2	1.3	(0.2 - 4.7)
Builder	1	1.3	(0.0 - 7.2)
Electrician's mate	3	1.2	(0.2 - 3.5)
Hospital corpsman	5	1.2	(0.4 - 2.8)
Machinist's mate	5	0.9	(0.3 - 2.1)
Cryptologic technician	2	0.9	(0.1 - 3.2)
Yeoman	2	0.8	(0.1 - 2.9)
Aviation ordnanceman	1	0.8	(0.0 - 4.5)
Fireman†	2	0.7	(0.1 - 2.5)
Sonar technician	1	0.7	(0.0 - 3.9)
Seaman	5	0.7	(0.2 - 1.6)
Radioman	2	0.6	(0.1 - 2.2)
Fire control technician	1	0.5	(0.0 - 2.8)
Electronics technician	2	0.5	(0.1 - 1.8)
Hull technician	1	0.4	(0.0 - 2.2)

Aviation electronics technician	1	0.4	(0.0 - 2.2)
Aviation machinist's mate	1	0.3	(0.0 - 1.7)
Unknown	1	--	--
 Total	 68	 0.7‡	 (0.5 - 0.9)

*ASW, anti-submarine warfare.

†Navy firemen work in hot boiler and engine rooms, and are not equivalent to civilian firemen.

‡Statistically significant at the $p < 0.05$ level.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Incidence of non-Hodgkin's lymphomas was examined in a prospective study of all white U.S. Navy enlisted men (average annual population = 435,425) during 1974-83 to test for existence of any short-term risk possibly related to occupation. Men in 80 occupations, ranging from clerk and journalist to machinist and boiler operator were observed for 3,704,864 person-years; mean length of service was 5.1 years, but 19 percent of person-years were contributed by men who had served at least 11 years. A total of 103 cases were detected during active service. Examination of pathology records and specialist board reviews.		

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confirmed 68 cases: 44 diffuse (25 histiocytic, 6 poorly differentiated lymphocytic, 4 well-differentiated lymphocytic, 4 mixed lymphocytic-histiocytic, and 5 undifferentiated pleomorphic); 13 nodular (10 poorly-differentiated lymphocytic and 3 mixed lymphocytic-histiocytic); and 11 unspecified or other. The annual age-adjusted incidence rate of confirmed cases per 100,000 person-years in men aged 17-64 years was significantly lower than in men the same age in the U.S. SEER population, possibly due to a healthy worker effect. Risk was unrelated to length of service, and no occupational group in the Navy showed a significant excess. The latency periods of the non-Hodgkin's lymphomas are unknown. It was not possible in this study to examine the long-term (greater than 20 years) occupational risk for non-Hodgkin's lymphomas. These results indicate that risk according to occupation is not expressed in the short term. —

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